HEART RATE VARIABILITY ANALYSIS FOR PATIENTS WITH OBSTRUCTIVE SLEEP APNEA

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Abstract - **Obstructive sleep apnea (OSA) is a common health concern associated with serious implications and increased cardiovascular morbidity and mortality. This study approaches the problem of identification OSA patients and detection of OSA phases on the basis of heart rate variability (HRV) analysis. Only a single ECG-channel is required for this purpose. We used data from the apnea ECG database [6]: 40 patients with documented OSA and 20 controls divided into a learning and a test set of equal size. Commonly used HRV measures as well as some novel parameters are tested. The results are compared by ROC-analysis and promising parameters are combined into a multidimensional vector and evaluated by means of a second order polynomial classifier. Best results are obtained from parameters calculated by time delay embedding and correlation analysis of the interbeat interval series. For the identification task, 95% sensitivity and 100% specitifity are achieved on the independend test set. The detection task yields an average classification rate of almost 85 %.**

Keywords **– Heart rate variability, obstructive sleep apnea, time delay embedding, correlation analysis.**

I. INTRODUCTION

Obstructive sleep apnea (OSA) is frequently associated with a variety of health implications: from moderate problems with breathing and snoring during night, daytime drowsiness up to severe restrictions in the cardiovascular system we find a wide range of different degrees of this illness. Mostly middle aged males are affected with an estimated prevalence of about 4% [1]. The clinical method of polysomnography is currently used for diagnosing OSA [2]. This procedure is time-consuming and expensive and requires the patient's stay overnight in hospital in a specially equipped sleep laboratory for recording of different biosignals, e.g. respiratory and cardiovascular signals, the electroencephalogram, vital parameters etc.

Meanwhile, there is some evidence that the cardiac rhythm respectively the time course of heart rate shows some specific patterns which occur frequently with OSA. These patterns are reported by several authors [3, 4] as cyclic variations with particularly high amplitude modulation corresponding to phases of apnea and bradycardia followed by an increase in heart rate and the corresponding stop of apnea. Fig 1. demonstrates such a characteristic heart rate pattern for about 7 minutes from an OSA patient. Because of these findings Guilleminault [3] suggested to evaluate a simple screening method for the existence of OSA taking these cyclic patterns into consideration.

The aim of our study follows this idea and is performed in two different steps: i.) (Identification) what means, to investigate, if patients with OSA could be identified from healthy subjects by means of heart rate variability parameters,

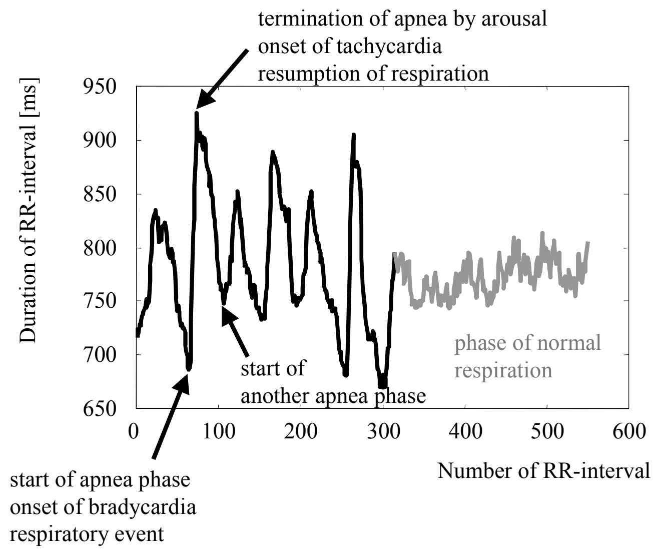

Fig.1. Sequence of RR intervals recorded from a patient with obstructive sleep apnea. The first half of the time course shows several apnea phases where as the second half has a normal characteristic.

and ii) (Detection) if for those patients phases of apnea during sleep could be detected by heart rate variability analysis of Holter ECGs. For both questions the information of only one electrocardiogram (ECG) channel is available. We tested many well known parameters in time and frequency domain [5] as well as some new ones based on time delay embedding and correlation analysis. The performance of all features considered in this evaluation is assessed by ROC analysis. However, in this study we only report about the most meaningful parameters which yielded best results in terms of sensitivity and specificity. In order to increase the classification performance, a multidimensional feature vector is tested by a polynomial classifier.

II. METHODOLOGY

Our investigation is carried out on a sample of 40 patients with established OSA and 20 healthy control probands [6]. For all subjects of this study one single ECG channel is recorded overnight for about 8 hours. The 60 records are equally divided into a training and a test set of 20 patients, respectively 10 controls. Healthy controls have fewer than 5 minutes with apnea. The record of a patient contains at least one hour with an apnea index of 10 or more, and at least 100 minutes with apnea during the recording. All apneas are either obstructive or mixed. Hypopneas are also counted as apneas. More details can be found in [6].

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In the training set, file by file information on the proband's status (patient/control) as well as minute by minute annotations on the occurrence of apnea at the beginning of this minute are available. The annotations were made by human experts on the basis of simultaneously recorded respiration signals. For the data in the tests set, no further information is given.

The ECG signal is recorded with a sampling frequency of 100 Hz and 12 bit resolution. All parameters quantified in this study are derived from the sequence of RR intervals of the ECG signals. In order to increase the time-resolution of the original data, the ECG signal is first interpolated using cubic splines and then resampled with 1000 Hz. A median highpass filter (width 501 ms) to reduce baseline wander is then applied. After R peak detection, a classification of QRS-morphology [7] and -timing is performed to identify artefacts and ectopic beats and exclude them from further processing. Gaps in the RR-sequence resulting from rejected or missing beats are interpolated by means of a nonlinear algorithm described in [8].

In correspondence to the two goals of *identification* and *detection* further processing of the data follows different procedures.

Detection of apnea phases is performed on the corrected RR sequence which is cut into successive segments of one minute in duration. For each segment the corresponding HRV measures are estimated and finally smoothed by median filtering.

Parameters for *identification* of patients with established apnea are calculated in two different kinds: i) the HRV parameters are estimated at once from the total signal of about 8 hours; and ii) from the mentioned detection measures calculated for successive one minute segments the median is taken as representative feature for the whole signal.

We calculated for both procedures the commonly used HRV time domain parameters [5]: standard deviation (SD) of all RR intervals between successive beats of normal origin (NN intervals), (SDNN), the absolute (NN50count) and relative (pNN50) number of successive pairs of NN-intervals that differ more than 50 ms and the square root of the mean of the summed squares of differences between adjacent NN-intervals (RMSSD), the SD of the mean of the NN intervals in all 5-minute segments of the recording (SDANN) and the mean of the SD of all NN intervals for all consecutive 5-minute segments (SDNN index).

Another time dependent parameter for HRV analysis is introduced as the so called correlation based feature (CBF). It is calculated within RR interval segments of 5 minute duration, which are shifted in increments of 1 minute over the whole signal. See Fig. 2.

From each 5 minute segment, the central window of one minute duration is extracted and cross correlated with the surrounding 5 minute segment. The sum of all normalized correlation values that exceed the threshold 0.45 yield the value of CBF. It aims to identify the cyclical variation of heart rate described in [3].

In addition to these parameters, we investigated two features that have been proposed in EEG processing for

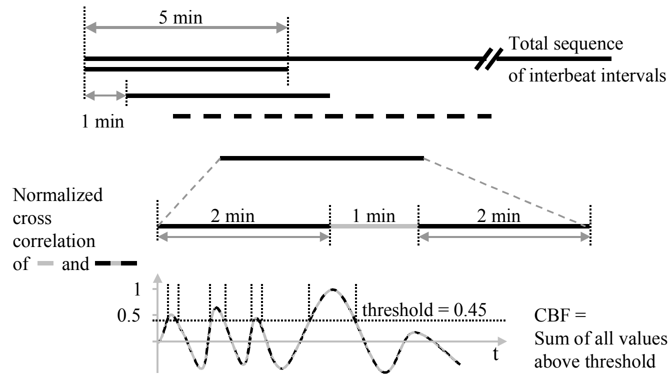

Fig.2 Calculation of the Correlation Based Feature (CBF)

brain-computer interfacing [9] and which are not commonly used in HRV analysis. Both features are derived from the time delay embedded corrected series of RR intervals. Given that the time segment of analysis contains N RR-intervals x_i (i=1..N), embedding vectors $\vec{x}_i$ of the dimension D are constructed from values x_i that are spaced t RR intervals apart:

$$\vec{x}_i = \left(x_i \quad x_{i+t} \quad \cdots \quad x_{i+(D-1)\cdot t}\right)^T$$

In [9], the vectors $\vec{x}_i$ directly form the columns of the embedding matrix X. In our realisation, we first calculate the mean vector $\vec{m}$ of all embedding vectors $\vec{x}_i$

$$\vec{m} = \frac{1}{N-(D-1)\cdot t} \sum_{i=1}^{N-(D-1)\cdot t} \vec{x}_i$$

and subtract it from each vecor $\vec{x}_i$ prior to the aggregation. So, the embedding matrix X is calculated according to

$$X = \left[\vec{x}_1 - \vec{m} \quad \vec{x}_2 - \vec{m} \quad \cdots \quad \vec{x}_{N-(D-1)\cdot t} - \vec{m}\right]$$

The sorted eigenvalues l_i of the DxD-Matrix $X \cdot X^T$ are the basis for our parameters

$$l_1 \cdots l_D = Eigenvalues\left(X \cdot X^T\right)$$

$$\text{where} \quad l_i > l_{i+1} \quad \text{for } i = 1 \cdots D-1$$

The magnitude of each eigenvalue is normalized with respect to the sum of all eigenvalues:

$$\lambda_i = \frac{l_i}{\sum_{i=1}^{D} l_i}$$

and the normalized maximal eigenvalue (NME) serves as classification feature:

$$NME = \lambda_1$$

Since, up to a multiplicative constant, the matrix $X \cdot X^T$ is identical to the covariance matrix of the vecors $\vec{x}_i$, NME reflects the extension of the cluster of the embedded RR series in the direction of its largest extension relative to its 'size' in the directions of the other eigenvectors.

The second parameter is derived from the Entropy H of the embedding space eigenspectrum

$$H = -\sum_{i=1}^{D} \lambda_i \cdot ld\left(\lambda_i\right)$$

It is calculated following [9] as $EBF = 2^H$ and quantifies the so called stochastic 'complexity' of the underlying time series.

In this study, the values for the embedding Dimension D and time delay t were empirically set to 3. It should be noted, that the resulting numbers of NME and EBF do not reflect 'true values' in the sense of the theory of nonlinear dynamics, where an embedding dimension D sufficiently high for the underlying attractor must be guaranteed. Rather, they describe spatial properties of the cluster formed by the embedding vectors. For classification purposes, the most important question is, whether these values have different distributions in the case of apnea segments and non apnea segments, regardless of whether the values are correct in a theoretical sense.

To assess the quality of the calculated parameters with respect to the classification task, ROC curves are generated for each measure by plotting sensitivity against (1-specificity) for all possible decision thresholds.

Furthermore, up to three different features are combined and the training set served to train a second order polynomial classifier which was used to reclassify the training set. For the best combination, a validation was performed on the tests set.

III. Results

ROC curves are used to characterize the quality of the single HRV features with respect to the identification task. The threshold corresponding to the point of the curve closest to the upper right corner (0,1) was considered as value that achieves best separation between the two groups. Table 1 shows the optimal values of sensitivity and specificity for all single HRV features considered in the classification procedure.

The first two columns, sensitivity and specificity, left side of Table I, are calculated for the total signal and the two columns to the right side present the median of the features based on the one min. segments.

Furthermore, the first three features NME, EBF and CBF, which do not belong to the standard HRV parameters,

TABLE I
CLASSIFICATION RATES FOR IDENTIFICATION OF OSA PATIENTS

	Analysis of total signal		Median of minute segments		
	Training set		Training set		Tests set
Parameter	Sens.	Spec.	Sens.	Spec.	Total
NME	85	70	95	100	28/30
EBF	75	80	95	100	27/30
CBF			95	100	28/30
pNN50	90	70	90	70	
NN50count	75	70	80	70	
SDNN	60	70	55	60	
SDSD	70	70	75	70	
RMSSD	70	70	75	70	
SDANN	60	80			
SDNN-index	60	70			

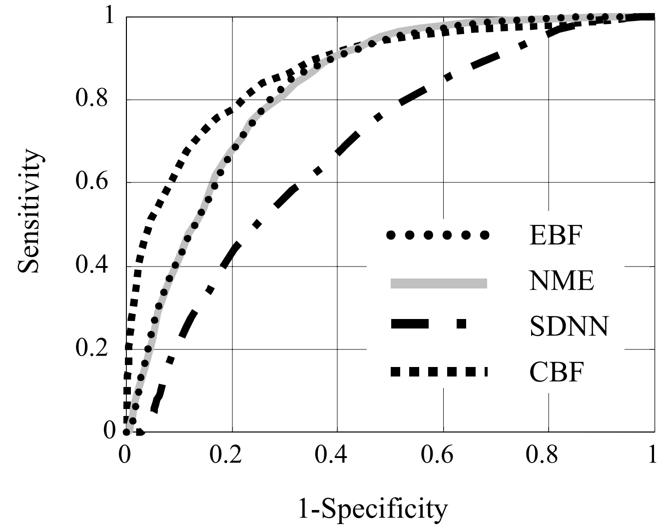

Fig.3 ROC Curves for Detection of OSA patients by CBF, NME, EBF and SDNN features, based on one minute ECG segments

achieve best results for the training sets compared to the standard time domain HRV parameters.

From this point of view the second detection task of apnea phases is continued with an emphasis on these three favourite features.The ROC-curves of Fig. 3 demonstrate the results achieved for minute by minute classification in the detection task. Obviously, the correlation based feature CBF achieves the best performance. However, the NME and EBF parameter are only slightly worse.

Table II shows the corresponding classification rates achieved for the minute by minute classification.

Slightly higher classification values resulted from application of selected feature combinations to a second order polynomial classifier. Up to three features are tested (Table III).

TABLE II
CLASSIFICATION RATES FOR DETECTION OF OSA PHASES

	Training set	
Parameter	Sens	Spez
NME	76.73	74.76
EBF	81.33	72.05
CBF	81.31	77.16
SDNN	68.57	58.93

TABLE III
CLASSIFICATION RATES FOR DETECTION OF OSA PHASES.
COMBINATIOPN OF UP TO THREE FEATURES.

	Training set	
Combination	Sens	Spec
CBF / NME	72.22	87.38
CBF / EBF	74.11	84.30
NME / SDNN	74.96	87.09
CBF / NME / SDNN	73.36	89.33

IV. Discussion

The best single parameter in the OSA *detection task* was found to be CBF. With a sensitivity of 81,3%, identical to that of EBF it has a better specificity 77.2% than the other features and yields on average 79.1% correct classification on the tests set. Slightly worse results are obtained from the embedding based features.

The comparatively regular structure of the RR intervals during apnea phases [3] is better captured by the NME, EBF and CBF features. Especially CBF has the advantage that its magnitude is only based on similarity of the RR intervals on a short timescale (5 min) and therefore allows for variability of the cyclic variation of heart rate pattern even in the same patient, largely independent from its amplitude and frequency. The same would be expected for NME and EBF, however only in the limit of a long data sequence and an embedding dimension sufficiently high, which is not given here due to the restriction to analysis segments of one minute in duration.

From visual inspection, a *detection* of the apnea phases using SDNN seems feasible within one patient, however the high inter-patient variability and the fact that SDNN is generally higher in healthy persons does not allow to use a fixed threshold.

The best results in the *identification* of patients with OSA (95% sensitivity, 100% specificity on the training set, up to 28/30 on the tests set) are also obtained from the features CBF, NME and EBF (Table I). Interestingly, these results are only achieved when the median minute by minute values are considered. Calculation over the whole signal duration decreases the performance considerably, because the higher regularity of the cyclic variations of heart rate during periods of apnea is blurred by other fluctuations. From the established HRV measures, pNN50 yields the best results (90% sensitivity, 70% specificity). Generally, lower, less complex heart rate variability is found in apnea patients.

The combination of several features allows to improve the results (Table III). Using three features – CBF, NME and SDNN – an average classification rate of almost 85% was achieved on the tests set.

Generally, the temporal smoothing of the minute by minute values and classification results by means of a median filter yielded a considerable improvement of the classification rates. Best results are achieved using a width between 9 and 15, indicating that apnea phases often extend over several minutes. The filter successfully suppressed spurious short term transgressions of the decision threshold.

Further improvements may be expected from the combination of *identification* and *detection* i.e. by attempting a detection procedure only on subjects which are identified as OSA patients. This may lead to an improvement of detection sensitivity which is probably too low (< 80 %) for practical purposes.

In summary, our results obtained are very promising and indicate, that much – if not all – of the information necessary to diagnose sleep apnea is contained in the ECG signal.

Further investigations will have to be carried out in order to confirm the diagnostic performance in presence of other diseases.

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